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# Indicators of quality use of medicines in South-East Asian countries: a systematic review

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## Abstract

**OBJECTIVES** To identify indicators of quality use of medicines used in South-East Asian region.

**METHODS** A systematic review was conducted searching MEDLINE, Embase and The International Network for Rational Use of Drugs (INRUD) and The World Health Organization (WHO) website. Original studies or reports carried out in the South-East Asian region, explicitly using indicators to measure quality use of medicines, and published between January 2000 and July 2011 were included.

**RESULTS** A total of 17 studies conducted in 7 of 11 countries in South-East Asia were included. WHO indicators focusing on general medication use in health facilities were most widely used (10 studies). Twelve studies used non-WHO indicators for measuring quality use of medicines in clinical areas (geriatrics and obstetrics) or specific diseases, such as diarrhoea and pneumonia. In five studies, WHO indicators were used along with non-WHO indicators. There was little information available about validity, reliability and feasibility of the non-WHO indicators. The majority of indicators measured process rather than structure or outcome. There were very few indicators addressing non-communicable diseases.

**CONCLUSIONS** A limited number of studies have been published explicitly using indicators of quality use of medicines across South-East Asia. Importantly, existing indicators need to be complemented with valid, reliable and feasible indicators related to non-communicable diseases, particularly those with a high financial burden to meet the current medical challenges in the region.

**keywords** quality indicator, South-East Asia

## Introduction

WHO (2010) estimated that more than half of all medicines over the world were prescribed, dispensed or sold inappropriately. Examples of irrational use of medicines include use of too many medicines per patient (Hajjar *et al.* 2007), inappropriate use of antimicrobials (Werner *et al.* 2011) and failure to prescribe in accordance with clinical guidelines (Ko *et al.* 2010). Over three decades ago, the WHO in collaboration with the International Network for Rational Use of Drugs (INRUD) developed a set of indicators measuring quality use of medicines and prescribing behaviour in health facilities (Hogerzeil *et al.* 1993; WHO 1993). These indicators are widely accepted as an objective standard method to assess rational use of medicines and have been used in over 30 countries, mainly in the developing world (Laing *et al.* 2001; WHO 2004, 2009). Another set of WHO indicators addresses the pharmaceutical situation of countries including rational

medicine use (WHO 2007b). Finally, more recently, WHO has published a set of indicators for the use of medicines at household level (WHO 2007a, 2011). Apart from the widely used WHO indicators, measures of quality use of medicines for specific diseases like asthma or diabetes have been developed and applied in developed countries (Martirosyan *et al.* 2010; To *et al.* 2010). Indicators are a tool for policy-makers and healthcare managers to assess and monitor the extent of rational medicine use, to compare differences across facilities, districts or regions, to analyse changes over time and to evaluate interventions (Hogerzeil 1995; Quick *et al.* 1997; Laing *et al.* 2001; Majeed *et al.* 2007).

South-East Asia is a region consisting of eleven countries – Brunei, Singapore, Malaysia, Thailand, the Philippines, Indonesia, Vietnam, Laos, Cambodia, Myanmar and East Timor (PubMed definition). These countries have a common history, geography and position as a major crossroad of trade and the movement of goods and services. Recently,

a set of papers discussed health and related matters in South-East Asian countries as an emerging focus for global health (Acuin *et al.* 2011; Chongsuvivatwong *et al.* 2011; Coker *et al.* 2011; Dans *et al.* 2011; Kanchanachitra *et al.* 2011). The region is dealing with the challenge of an increase in non-communicable diseases associated with population ageing. The health systems are a mix of traditional medical practices and the use of new medical technologies and pharmaceutical products, presenting problems in terms of safety and quality. In addition, there is a rising demand for high-quality health care because of increasing educational levels and wealth as well as a growing consciousness of human rights in societies with a developing democratic environment. Although this series of papers addressed some aspects of quality of health care and challenges related to health insurance coverage, it did not address the quality use of medicines or explicit methods to measure quality, neither could we identify any other reviews on this topic. It remains unknown whether existing indicators are suitable for the current medical challenges. In this systematic review, we aimed to identify studies explicitly using indicators of quality use of medicines in the South-East Asian region answering the following three research questions: (i) which indicators have been used; (ii) what is known about the validity, reliability and feasibility of the existing indicators; and (iii) what are the main results based on of the commonly used indicators.

## Methods

### Search strategies

A systematic literature review was conducted according to the PRISMA instructions (Moher *et al.* 2009), using PubMed (MEDLINE) and Embase databases with relevant keywords: 'quality indicators, health care', 'quality indicator(s)', 'safety indicator(s)', 'indicator(s)', 'medication errors', 'drug monitoring', 'adverse drug reaction reporting systems', 'drug reporting system(s)', 'medical audit', 'quality assurance, health care', 'rational use', 'pharmaceutical preparations', 'medication', 'drug(s)', 'pharmaceutical sector', 'asia, southeastern', 'southeastern asia', 'southeast asia', and individual country names as MeSH terms and free-text words or combinations. We also performed searches in INRUD bibliography (The International Network for Rational Use of Drugs: <http://www.inrud.org>) and in the WHO (<http://www.who.int>) website with the keyword 'indicator(s)'. The searches were restricted by published date between January 2000 and July 2011, but not for languages.

Duplicated studies were eliminated. All remaining titles and abstracts were independently screened and selected by

two authors (H.T.N and K.T). Disagreements were resolved through discussion. Studies deemed relevant at the first screening were retrieved in full-text format and screened for further eligibility. Related articles and the reference lists of reviewed articles were searched for additional studies.

### Inclusion criteria

We included original studies or reports that (i) were carried out in South-East Asian region, (ii) explicitly used indicators to measure quality use of medicines including prescribing, dispensing and utilisation of medicines, adopted from official sources/sets (e.g. WHO documents) or clearly defined indicators (namely unambiguous descriptions and clear definitions of variables to be measured, explicit definition of the population to be included and the setting to which they apply) (Hearnshaw *et al.* 2001; Campbell *et al.* 2003; Hepler & Segal 2003) and (iii) were published between January 2000 and July 2011.

### Exclusion criteria

We excluded studies that (i) used exclusively other methods to describe/measure rational use of medicines rather than using indicators and (ii) did not provide sufficient details in methods and results sections, thus failing to answer research questions.

### Data abstraction

The following information was extracted: first author, publication year, country, design, study level (for example: national, provincial or hospital), setting and objective of study, number and description of indicators used. For studies including multiple indicators, we only included indicators addressing quality use of medicine and excluded those relating to other aspects of care (for instance, access to or quality of medicines). The first author extracted the data and the last one checked this.

### Data analysis

For each indicator of quality use of medicines, several parameters were determined. To assess the original source of the indicator, we checked whether indicators were developed by WHO or not. The latter were named non-WHO indicators. Similar indicators were grouped together. We classified indicators according to the dimension of quality of care as *structure* (defined as the capacity to provide high quality of care), *process* (referred to the actions of healthcare providers, such as prescribing,

dispensing, etc.) or *outcome* (including recovery, restoration of functionality, knowledge about therapy and survival of patients) indicators as described by Donabedian (Donabedian 2005), irrespective of the category defined in the original source, from which they were selected.

WHO indicators were developed by appropriate methods, well tested in many countries and applied in various studies in a standard way: the face and content validity, reliability and feasibility of those indicators have been proven (WHO 1993, 2006a, 2007a, 2009, Brudon *et al.* 1999). All other indicators were evaluated on the information provided in the studies and additional documents cited in the original papers as follows (Martirosyan *et al.* 2010):

- Content validity: indicators were based on the literature review or evidence-based clinical guidelines.
- Face validity: indicators were assessed and accepted by a group of experts or professionals in the field.
- Feasibility: feasibility of calculation of indicators was demonstrated or defended in the view of available data.
- Reliability: indicators yield the same outcome when measured by different persons at different times.

### The main results of most commonly used indicators

Results of commonly used indicators in the reviewed articles were extracted and aggregated if there were at least three results from different countries. We included the results of both WHO and non-WHO indicators if their contents were comparable and presented aggregated data as a range for each indicator.

## Results

In total, 696 potentially relevant articles were identified (PubMed: 376, Embase: 308, INRUD: 9 and WHO: 3). Of those, 19 original studies met the inclusion criteria and were included in our analysis. Three papers (Stenson *et al.* 2001a,b; Syhakhang *et al.* 2001) were from a serial publication relating to the same PhD research project and are referred to as one study by (Syhakhang 2002). No relevant studies were identified from searching the related articles and the reference lists of included studies. As a result, 17 different studies were included for review.

The greatest number of studies was carried out in Laos (five studies). Others were conducted in Singapore (three studies), Cambodia (two studies), Thailand (two studies), Philippines (two studies), Vietnam (two studies) and Malaysia (one study). The studies were performed at different levels: national (12 studies), regional (one study), provincial (three studies) and hospital (one study) using

two major designs: to describe the situation of medication use (10 studies) or to assess practice improvement/impact of a certain intervention (seven studies) (Table 1).

Four studies used indicators to assess the pharmaceutical sector: one measured financial access to essential medicines including only one indicator relating to medication dispensing (Saleh & Ibrahim 2005), while the other three investigated also geographical access to essential medicines, quality and rational use of medicine (Falkenberg *et al.* 2000; Paphassarang *et al.* 2002; Batangan & Juban 2009a). Another four studies described overall medicine use patterns comprising prescribing and dispensing practices or assessed the impact of an intervention on these issues in various health facilities (health centres, hospitals and pharmacies) (Chareonkul *et al.* 2002; Syhakhang 2002; Keohavong *et al.* 2006; Vang *et al.* 2006). Indicators were applied in different clinical areas including geriatrics and obstetrics as well as in specific diseases comprising malaria, diarrhoea, pneumonia, psychosis, asthma, tuberculosis and diabetes in seven studies (Wahlstrom *et al.* 2003; Mamun *et al.* 2004; Chong *et al.* 2006, 2008; Uchiyama *et al.* 2006; Liabsuetrakul *et al.* 2008; Kanchanaphibool *et al.* 2009). One study evaluated the effectiveness of an intervention in the utilisation of antibiotics (Chalker 2001). Finally, one study described medication use in households (Batangan & Juban 2009b) (Table 1).

### WHO indicators

About half of the studies (10 studies, 59%) applied indicators developed by the WHO with some studies slightly modifying the indicators to fit the specific contexts (Paphassarang *et al.* 2002; Syhakhang 2002; Vang *et al.* 2006; Batangan & Juban 2009a,b). For instance, Vang *et al.* (2006) had scored indicators based on a 10-point scale instead of using percentages or absolute numbers as recommended by WHO. Prescribing and dispensing practices at facility level were assessed by using indicators of quality use of medicines in health facilities (WHO 1993). Those indicators were developed a long time ago, updated various times and incorporated into the package for assessing country pharmaceutical situation (WHO 2007b). The use of medicines at home was measured by using another set of WHO indicators for the household survey (WHO 2007a). Most of the studies using WHO indicators measured processes, only few focused on structures and outcomes (Appendix 1).

### Non-WHO indicators

Twelve studies used non-WHO indicators, which were developed either by a national organisation or by the

**Table 1** Description of studies using indicators of quality use of medicines

No	Reference	Country	Study level	Study setting	Study design	Study objective	Number & description of indicator(s) used	Source of indicator(s)
1	(Paphassarang <i>et al.</i> 2002)	Lao PDR	National	Pharmaceutical sector in general (National drug policy (NDP))	Intervention (Implementation of NDP/regulatory intervention)	To assess the impact of the National Drug Policy program to get evidence for revising the policy.	Twenty nine indicators comprising 15 indicators for monitoring National Drug Policy (NDP), 10 Good Pharmacy Practice (GPP) indicators, and other four measuring the knowledge of NDP and its components. Some of them related to dispensing and prescribing practices. It is impossible to know the exact number of indicators measuring quality use of medicines since the full list of indicators was not reported in the study.	1, 2
2	(Stenson <i>et al.</i> 2001a; Stenson <i>et al.</i> 2001b; Syhakhang <i>et al.</i> 2001; Syhakhang 2002)*	Lao PDR	Provincial	Public and private pharmacies (in Savannakhet province)	Intervention (Regulatory intervention: inspections, information, distribution of documents and sanctions)	To describe the quality of the private pharmacy services in comparison with that of public pharmacy regarding to aspects of good pharmacy practices and rational use of drug and to assess the effectiveness of government regulation.	Twelve indicators covering aspects of Good Pharmacy Practice (GPP) and rational use of drugs (RUD). Among those, eight assessed prescribing and dispensing practices and two related to facility.	1, 2
3	(Wahlsrom <i>et al.</i> 2003)	Lao PDR	National	Provincial hospitals (management of malaria, diarrhea and pneumonia)	Intervention (Introduction of STGs, audit, feedback & discussions)	To evaluate the effects of an educational intervention to improve treatment practices of three common diseases including malaria, diarrhea and pneumonia.	Three indicators addressing diagnostic and treatment of malaria, diarrhea and pneumonia in accordance to standard treatment guidelines. Each had some components relating to medication use.	2

**Table 1** (Continued)

No	Reference	Country	Study level	Study setting	Study design	Study objective	Number & description of indicator(s) used	Source of indicator(s)
4	(Keohavong <i>et al.</i> 2006)	Lao PDR	National	Public health facilities (provincial and district hospitals and health centers)	Descriptive	To evaluate the rational use of drug (RUD) patterns with a focus on prescribing and dispensing practices.	Fourteen indicators measuring prescribing and dispensing practices.	1
5	(Vang <i>et al.</i> 2006)	Lao PDR	National	Drug and Therapeutics Committees (DTCs) in central and provincial hospitals	Intervention (audit, feedback & discussions)	To assess DTCs performance, to evaluate improvements of an educational intervention and to monitor subsequent practices.	Eight indicators for assessing DTC performance. Of which, one indicator related to quality use of medicines. Ten indicators for RUD and other three for adherence to Standard Treatment Guidelines.	1, 2
6	(Mamun <i>et al.</i> 2004)	Singapore	National	Geriatric / Nursing Homes	Descriptive	To identify the prevalence of polypharmacy and inappropriate medication use in nursing homes.	Two indicators for nursing home care comprising polypharmacy and inappropriate medication use.	2
7	(Chong <i>et al.</i> 2006)	Singapore	National (Institutional)	Institute of Mental Health	Intervention (Implementation of National treatment programme)	To evaluate the quality of care before and after the implementation of early psychosis intervention programme (EPIP).	Thirteen process indicators covering different domains of care. Of which, seven related to treatment with medication.	2
8	(Chong <i>et al.</i> 2008)	Singapore	National	Polyclinics (specialist outpatient clinics of government hospitals)	Intervention (Audit & feedback)	To assess the impact of Singapore National Asthma Program on drug prescription pattern.	One indicator focusing on drug prescribing for asthma.	2
9	(Charonkul <i>et al.</i> 2002)	Cambodia	Provincial	Health centers (primary health care)	Descriptive	To identify drug use problems and to evaluate prescribing and dispensing practice compared to desired national guidelines.	Eighteen indicators for evaluating quality use of medicines in general and in some specific diseases (diarrhea and acute respiratory infection).	1, 2
10	(Uchiyama <i>et al.</i> 2006)	Cambodia	National	Anti-tuberculosis (TB) drug management (public health facilities and private pharmacies)	Descriptive	To assess anti-TB drug management of service providers, out-patients and drug storekeepers; to document practices of anti-TB drugs in the public and private sector in the concept of procurement, availability and price.	Six indicators focusing on anti-tuberculosis drug management. Of which, two related to prescribing practice of service providers and knowledge of TB out-patients.	2

**Table 1** (Continued)

No	Reference	Country	Study level	Study setting	Study design	Study objective	Number & description of indicator(s) used	Source of indicator(s)
11	(Liabsuetrakul <i>et al.</i> 2008)	Thailand	Regional (Southern Thailand)	Obstetric units (university, regional and provincial hospitals)	Descriptive	To evaluate the quality of care for conditions of severe pre-eclampsia/eclampsia, obstructed labor, and postpartum hemorrhage in the 5 southernmost provinces of Thailand	Eighteen indicators for assessing quality of obstetric care, of which seven indicators concerning drug use.	2
12	(Kanchanaphibool <i>et al.</i> 2009)	Thailand	Hospital	Public tertiary hospital	Descriptive	To assess the quality of diabetes care	Seven indicators comprising quality of diabetes care, of which only one related to medication use for prevention of complications.	2
13	(Falkenberg <i>et al.</i> 2000)	Vietnam	National	Pharmaceutical sector in general.	Descriptive	To assess the Vietnamese pharmaceutical sector regarding the standard of the drug quality control system, availability of drugs and rational use of essential drugs in the private and public sectors.	Ten indicators for monitoring national drug policy (NDP). Of which, four covering the field of rational use of drugs.	1
14	(Chalker 2001)	Vietnam	Provincial	Commune Health Stations (primary health care) Pharmaceutical sector in general	Intervention (Conditional equipment donation) Descriptive	To evaluate antibiotic use pattern before and after an intervention.	Two drug-use indicators focusing on antibiotic use and dosage.	1, 2
15	(Batangan & Juban 2009a)	Philippines	National	Pharmaceutical sector in general	Descriptive	To assess Philippines pharmaceutical situation covering access, quality and rational use of medicines at health facility level.	Twenty five indicators for assessing, monitoring and evaluating country pharmaceutical situation. Of which, eighteen related to medication prescribing, dispensing and utilization.	1
16	(Batangan & Juban 2009b)	Philippines	National	Medication use at household	Descriptive	To measure access to and use of medicines at household level.	Five composite indicators for measuring aspects of access to and rational use of medicines at home. Of which, one addressing medication use at home.	1
17	(Saleh & Ibrahim 2005)	Malaysia	National	Pharmaceutical sector in the context of essential medicines list implementation	Descriptive	To assess the pharmaceutical sector to know whether people have access to essential medicines.	Four indicators focusing on availability and affordability of essential medicines. Of which, only one related to medication dispensing.	1

\* (Stenson *et al.* 2001a; Stenson *et al.* 2001b; Syhakhang *et al.* 2001) viewed as (Syhakhang 2002).  
 1, WHO indicator(s); 2, non-WHO indicator(s).



authors themselves. In five studies, non-WHO indicators were used along with the WHO indicators (Chalker 2001; Chareonkul *et al.* 2002; Paphassarang *et al.* 2002; Syhakhang 2002; Vang *et al.* 2006). Those indicators were categorised into four groups: (i) rational medicine use in general, (ii) quality of pharmacy practice (Good Pharmacy Practice (GPP) indicators), (iii) rational medicine use in specific clinical areas or diseases (Clinical area/disease-oriented indicators) and (iv) other aspects involving medication use (Appendix 2).

Few non-WHO indicators sets were judged to be face and content valid and reliable (Table 2). These indicators were developed based on experts' consensus and related to available literature or standard treatment guidelines and tested within local contexts. For instance, Good Pharmacy Practice (GPP) indicators were developed by Lao Food and Drug Department and tested for reliability in pharmacies (Paphassarang *et al.* 2002; Syhakhang 2002); or indicators assessing adherence to standard treatment guidelines of malaria, diarrhoea and pneumonia were developed in the Lao National Drug Policy (NDP) implementation programme and tested by the Department of Curative Medicine in a hospital (Wahlstrom *et al.* 2003). Most studies described indicators that were based on existing literature and/or clinical guidelines, and these were judged to have content

validity. Four studies did not provide any data or reported ambiguous messages on the process of developing and testing the indicators (Chalker 2001; Chareonkul *et al.* 2002; Paphassarang *et al.* 2002; Chong *et al.* 2008), so content and face validity could not be determined. All of the non-WHO indicators reported results and were therefore assumed to be feasible within the context of the specific study, except for the indicators assessing adherence to Lao standard treatment guidelines of malaria, diarrhoea and pneumonia as they were used in two distinct studies (Wahlstrom *et al.* 2003; Vang *et al.* 2006). However, the feasibility of all of these indicators on a larger scale was not tested. The exception was the Lao GPP indicator study which confirmed the feasibility of the indicators as they were regularly used for inspection of pharmacies in Laos (Paphassarang *et al.* 2002; Syhakhang 2002) (Table 2). Most of the non-WHO indicators identified were process, followed by structure and outcome indicators (Appendix 2).

#### Summary results of most commonly used indicators of quality use of medicines

Only a limited number of studies used indicators that allow comparison of results across countries. Among the identified indicators, the most prominent ones were

**Table 2** Evaluation of non-WHO indicators of quality use of medicines\*

Indicators	Evaluation Content validity	Face validity	Feasibility	Reliability
1. Rational medicine use in general				
Antibiotic use (Chalker 2001)	–	–	±	–
Medicine use in hospital (Vang <i>et al.</i> 2006)	–	+	±	–
Patient care and facility (Chareonkul <i>et al.</i> 2002)	–	–	±	–
2. Good pharmacy practice (GPP) indicators (Syhakhang 2002; Paphassarang <i>et al.</i> 2002)				
Facility specific indicators	+	+	+	+
Dispensing indicators				
3. Clinical area/disease-oriented indicators				
Geriatrics (Mamun <i>et al.</i> 2004)	+	–	±	–
Obstetrics (Liabsuetrakul <i>et al.</i> 2008)	+	–	±	–
Malaria, diarrhea and pneumonia (Chareonkul <i>et al.</i> 2002)	+	–	±	–
(Vang <i>et al.</i> 2006; Wahlstrom <i>et al.</i> 2003)	+	+	±	+
Asthma (Chong <i>et al.</i> 2008)	–	–	±	–
Diabetic (Kanchanaphibool <i>et al.</i> 2009)	+	–	±	–
Psychosis (Chong <i>et al.</i> 2006)	+	–	±	–
Tuberculosis (TB) (Uchiyama <i>et al.</i> 2006)	+	–	±	–
4. Others				
National Drug Policy (NDP) (Paphassarang <i>et al.</i> 2002)	–	–	±	–
Drug and Therapeutics Committee (DTC) (Vang <i>et al.</i> 2006)	+	–	±	–

(+), Positive information; (–), No/ambiguous information; (±), Limited information.

\*List of non-WHO indicators used in the included studies is provided in Appendix 2.



**Table 3** Results of most commonly used indicators in Southeast Asia

Indicators	Results*
<b>General prescribing indicators</b>	
Average number of medicines per encounter/prescription/patient (Syhakhang 2002; Paphassarang <i>et al.</i> 2002; Falkenberg <i>et al.</i> 2000; Batangan & Juban 2009a; Chareonkul <i>et al.</i> 2002; Keohavong <i>et al.</i> 2006)	1.4–3.8
Percentage of medicines prescribed by generic name (Syhakhang 2002; Batangan & Juban 2009a; Chareonkul <i>et al.</i> 2002; Keohavong <i>et al.</i> 2006)	35.0–99.8
Percentage of encounters/patients with an antibiotic prescribed (Syhakhang 2002; Paphassarang <i>et al.</i> 2002; Batangan & Juban 2009a; Chareonkul <i>et al.</i> 2002; Keohavong <i>et al.</i> 2006; Chalker 2001)	13.1–66.0†
Percentage/number of encounters/patients with an injection prescribed (Syhakhang 2002; Paphassarang <i>et al.</i> 2002; Falkenberg <i>et al.</i> 2000; Batangan & Juban 2009a; Chareonkul <i>et al.</i> 2002; Keohavong <i>et al.</i> 2006)	1.3–32.0
Percentage of medicines prescribed from essential medicines list or formulary (Syhakhang 2002; Paphassarang <i>et al.</i> 2002; Batangan & Juban 2009a; Chareonkul <i>et al.</i> 2002; Keohavong <i>et al.</i> 2006)	56.0–99.7
<b>Prescribing indicators for treatment simple diarrhea in children under age 5</b>	
Percentage of patients prescribed Oral Rehydration Salts/Solutions (ORS) (Paphassarang <i>et al.</i> 2002; Batangan & Juban 2009a; Chareonkul <i>et al.</i> 2002; Keohavong <i>et al.</i> 2006)	60.0–100.0†
Percentage of patients prescribed antibiotics (Paphassarang <i>et al.</i> 2002; Batangan & Juban 2009a; Chareonkul <i>et al.</i> 2002; Keohavong <i>et al.</i> 2006)	22.0–81.3†
Percentage of patients prescribed anti-diarrheal /antispasmodic drugs (Paphassarang <i>et al.</i> 2002; Falkenberg <i>et al.</i> 2000; Batangan & Juban 2009a; Keohavong <i>et al.</i> 2006)	0.0–30.0
<b>Dispensing/patient care indicators</b>	
Percentage of medicines dispensed/received/administered (Saleh & Ibrahim 2005; Batangan & Juban 2009a; Chareonkul <i>et al.</i> 2002; Keohavong <i>et al.</i> 2006)	84.8–100.0
Percentage of medicines adequately labeled (Batangan & Juban 2009a; Chareonkul <i>et al.</i> 2002; Keohavong <i>et al.</i> 2006)	0.0–97.1
Patients' knowledge of correct dosage/how to take medicines (Batangan & Juban 2009a; Chareonkul <i>et al.</i> 2002; Keohavong <i>et al.</i> 2006)	55.0–80.0

\*Due to small number of studies, only ranges are presented.

†Included the results of non-WHO indicators whose contents were comparable to those of WHO indicators.

indicators addressing prescribing and dispensing/patient care practices of healthcare providers (Table 3).

Rational medicine use in general was measured in seven studies. The overall results showed wide variation for all indicators involved, often with about twofold differences. For example, the number of medicines per prescription ranged from 1.4 to 3.8. The percentage of medicines prescribed from the essential medicine list was encouraging in some health facilities with a percentage of nearly 100.0, but still poor in other studied sites (56.0%). The most extreme difference was the percentage of encountering an injection, which was 1.3% in Laos (Paphassarang *et al.* 2002) and 32.0% in Vietnam (Falkenberg *et al.* 2000).

Appropriateness of medicine use for treatment of a specific disease, that is, diarrhoea, in children under 5-year old was addressed in five studies. The findings varied between 60.0 and 100.0%, 22.0–81.3% and 0.0–30.0% of patients with simple diarrhoea prescribed oral rehydration salts/solutions (ORS), antibiotics and antidiarrhoea/antispasmodic drugs, respectively.

Quality of medication dispensing or patient care was assessed in four studies. Most patients (55.0–80.0%) knew

how to take medicines in the majority of cases (84.8–100.0%) studied. However, labelling medicines broadly varied from not being labelled at all to almost adequate.

## Discussion

A total of 17 studies conducted in seven countries in South-East Asia using indicators of quality use of medicines were included in this review. WHO indicators mainly focusing on general medication use in health facilities were most frequently used. New indicators for measuring quality use of medicines in specific clinical areas/diseases have been developed with little information on their validity, reliability and feasibility. The majority of indicators identified measured process, followed by structure and outcome.

We did not find studies from Brunei, Indonesia, Myanmar and East Timor. Furthermore, with the exception of Laos, only few studies were performed in each country. One of the reasons may be that these are mainly developing countries (except for Singapore) where electronic medical records and insurance data are often absent and monitoring of medicine use is not undertaken (Holloway & Van

Dijk 2011). Also, scientific journals may not be interested in publishing studies on routine monitoring of drug utilisation. Based on the limited data, quality use of medicines in South-East Asia was suboptimal and varied greatly. Some of the comparisons are restricted because target values for indicators are not available or depend on local practices. In view of the sparse data, it was not feasible to conduct statistical analysis. We found that between 1.4 and 3.8 medicines were prescribed per encounter, which is only partly in line with the range of 2.0–2.7 identified in a recent large study (WHO 2009). A value of two was suggested to be adequate (Chareonkul *et al.* 2002; Batangan & Juban 2009a), but five studies reported a value of more than two (Falkenberg *et al.* 2000; Chareonkul *et al.* 2002; Paphassarang *et al.* 2002; Syhakhang 2002; Keohavong *et al.* 2006). The percentage of prescriptions with an antibiotic or with an injection also varied widely; a threshold of not more than 30% has been recommended for injection (WHO 1993). Differences could be because of disease patterns, health policies (e.g. effort to improve prescribing pattern) and culture. For example, the rate of injections per prescription in the study by Falkenberg was probably high, because many patients, especially in mountainous areas, expected injections of vitamins (Falkenberg *et al.* 2000). Medicine use for the treatment of a disease (in children under 5-year old) was also suboptimal: not all patients with simple diarrhoea were prescribed ORS, but were given antibiotics and antidiarrhoea/antispasmodic drugs. These results were in line with the findings of a recent study at global level (WHO 2009). The most frequently used indicators were the ones developed by the WHO, especially the core set of indicators (WHO 1993). This is a well-accepted, highly standardised simple tool for fast and reliably assessing general medicine use, recommended for application in any medicine use study. The indicators for common specific diseases (including acute diarrhoea, acute respiratory infection and malaria) described in the annex (WHO 1993) were not used. Studies addressing the latter used indicators from other sources or developed their own (Falkenberg *et al.* 2000; Chareonkul *et al.* 2002; Paphassarang *et al.* 2002; Keohavong *et al.* 2006; Batangan & Juban 2009a). Three studies used WHO indicators for monitoring national drug policies (NDP) including indicators for rational use of medicines (Falkenberg *et al.* 2000; Paphassarang *et al.* 2002; Saleh & Ibrahim 2005). The two sets of indicators mentioned previously were further developed and incorporated into the WHO package of indicators for assessing, monitoring and evaluating country pharmaceutical situations (WHO 2006b), which were applied in two studies (Keohavong *et al.* 2006; Batangan & Juban 2009a). Only one study used WHO indicators for the household survey to measure quality use of medicines at

home (Batangan & Juban 2009b), possibly because this set is rather new (WHO 2007a, 2011).

More studies are needed using WHO indicators to assess quality use of medicines in the region to fill the gap in knowledge as highlighted previously. However, current WHO indicators do not address the recent changes of the health situation in the region with increasing chronic diseases and ageing population. They should be complemented with indicators related to non-communicable diseases, particularly those with a high financial burden. Encouragingly, there are some studies measuring quality use of medicines in specific medical fields (geriatrics and obstetrics) or in specific diseases (psychosis, asthma, tuberculosis, diabetes). However, they were mostly used in the context of a single study with insufficient information to assess their validity and reliability (Mamun *et al.* 2004; Chong *et al.* 2006, 2008; Uchiyama *et al.* 2006; Lia-bsuetrakul *et al.* 2008; Kanchanaphibool *et al.* 2009). Indicators should be developed using appropriate methods, for example, RAND (Campbell *et al.* 2003). Standard sets of valid and reliable indicators should be used in studies evaluating medication use to generate consistent data to facilitate the comparison across countries or regions. Indicators can then serve as a tool to revise medicine policies and to develop strategies for enhancing quality use of medicines at both national and regional levels.

Most indicators were process indicators rather than structure or outcome indicators. This is not surprising as most indicators assessed rational use of medicines, which is by definition a process indicator (Mainz 2003; Donabedian 2005). In general, structures are often readily formulated and easily measured, but are not always associated with better processes that yield the desired health outcomes. There is more evidence that process indicators are linked with outcome, but even this is not true for all situations (Sidorenkov *et al.* 2011). Furthermore, the process of care is in the control of healthcare providers and reflects their quality of care provision. Process indicators are therefore well suited to identify areas of possible change and to evaluate interventions. Outcomes are not always direct measures of the quality of health care provided and are likely to be influenced by patient-related factors (e.g. severity of the disease, patient age) and may take a very long time to occur (e.g. mortality or target blood pressure in hypertension) (Mainz 2003; Donabedian 2005).

### Strengths and limitations of the review

There is no defined keyword for 'indicator(s) of quality use of medicines'. We combined all potentially relevant MeSH terms and free-text terms. We found no additional studies searching the related articles or screening the lists of

references of included studies, indicating we have included the studies that met our inclusion criteria, in correspondence with the aim of the study. Secondly, we excluded studies on rational use of medicines in which the authors did not use the concept of indicator explicitly, for example Chuc *et al.* (2001) or Ayuthya *et al.* (2003). A complete overview of rational use of medicines in South-East Asia was outside the scope of the present study. Thirdly, there are inconsistencies in the definition of South-East Asia in the literature. The WHO has divided this area into two subregions, South-East Asia consisting of Indonesia, Myanmar, Thailand and East Timor and Western Pacific encompassing Brunei, Cambodia, Laos, Malaysia, Philippines, Singapore and Vietnam. Others included ten countries as members of ASEAN organisation, which excludes East Timor (Chongsuvivatwong *et al.* 2011). We considered South-East Asia as a region covering eleven countries, ten ASEAN members and East Timor, using the PubMed categorisation. Lastly, we did not search for unpublished papers or grey literature because of feasibility and resources. In an attempt to seek relevant locally published studies, one of the authors (H.T.N, Vietnamese) carried out a manual search of the relevant pharmaceutical and medical journals published in Vietnamese, but no studies were identified.

In conclusion, a limited number of studies have been carried out using indicators of quality use of medicines across South-East Asia. WHO indicators focusing on general medication use in health facilities were mainly used. Non-WHO indicators often lacked information on validity, reliability and feasibility. As far as results could be compared between studies, suboptimal quality use of medicine is indicated. Most importantly, existing indicators need to be complemented with valid, reliable and feasible indicators related to non-communicable diseases, particularly those with a high financial burden to meet the current medical challenges in the region.

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**Appendix I** List of WHO indicators used in reviewed articles

Type of indicators	St	Pr	Ot	References
Indicators of quality use of medicines at health facility level	2	17	1	
Prescribing indicators in general				
Average number of medicines per encounter/prescription/patient		X		(Keohavong <i>et al.</i> 2006; Paphassarang <i>et al.</i> 2002; Syhakhang 2002; Vang <i>et al.</i> 2006; Chareonkul <i>et al.</i> 2002; Chalker 2001; Falkenberg <i>et al.</i> 2000; Saleh & Ibrahim 2005; Batangan & Juban 2009a)
Percentage of medicines prescribed by generic name		X		
Percentage of encounters/patients with an antibiotic prescribed		X		
Percentage/number of encounters/patients with an injection prescribed		X		
Percentage of medicines prescribed from essential medicines list or formulary		X		
Number of medicines from the national essential medicines list, out of the 50 best-selling medicines in the private sector		X		
Percentage of prescription medicines bought with no prescription		X		
Prescribing indicators for specific diseases				
Simple diarrhoea in children under age 5				
Percentage of patients prescribed oral rehydration salts/solutions (ORS)		X		
Percentage of patients prescribed antibiotics		X		
Percentage of patients prescribed anti-diarrheal /antispasmodic drugs		X		
Mid/moderate pneumonia in children under age 5				
Percentage of patients prescribed first-line antibiotics		X		
Percentage of patients prescribed more than one antibiotic		X		
Non-pneumonia (flu) in patients of any age				
Percentage of patients prescribed antibiotics		X		
Dispensing/patient care indicators				
Average consultation time		X		
Average dispensing time		X		
Percentage of medicines dispensed/received/administered		X		
Percentage of medicines adequately labelled		X		

**Appendix 1** (*Continued*)

Type of indicators	St	Pr	Ot	References
Patients' knowledge of correct dosage/how to take medicines			X	
Facility indicators				
Availability of copy of essential medicines list or formulary	X			
Availability of standard treatment guidelines at public health facilities	X			
Indicators of quality use of medicines at household level	0	0	1	
Rational use of medicines at home*			X	(Batangan & Juban 2009b)

St, structure; Pr, process; Ot, outcome; The classification of structure, process and outcome indicators based on the aspect of care as described by Donabedian.

\*It was not reasonable to list individual indicators; Full lists of indicators used in original articles were not shown; only indicators relating to quality use of medicines were reported.

**Appendix 2** List of non-WHO indicators used in reviewed articles

Type of indicators	St	Pr	Ot	References
1. Rational medicine use in general	1	6	1	
Antibiotic use				
Antibiotic dose (% of patients receiving an adequate antibiotic dose)		X		(Chalker 2001)
Medicine use in hospital				
Medicine in hospital	X			(Vang <i>et al.</i> 2006)
Clear writing		X		
Traditional medicine		X		
Rational use of antibiotic		X		
Rational use of injection		X		
Patient care and facility				
Percentage patients confirmation of medicine instruction			X	(Chareonkul <i>et al.</i> 2002)
Use pictogram (plastic bag)		X		
2. Good pharmacy practice (GPP) indicators	2	3	0	
Facility specific indicators				
Order in the pharmacy	X			(Paphassarang <i>et al.</i> 2002;
Essential materials available in the pharmacy	X			Syhakhang 2002)
Dispensing indicators				
Labelling		X		
Mixing of medicines		X		
Information/percentage of informed customers		X		
3. Clinical area/disease-oriented indicators	0	23	1	
Geriatrics				
Polypharmacy (an order of $\geq 5$ medications per resident)		X		(Mamun <i>et al.</i> 2004)
Inappropriate medication use (based on established criteria by Beers MH and Strand LM)		X		
Obstetrics				
Seizure treatment and prophylaxis with magnesium sulphate		X		(Liabsuetrakul <i>et al.</i> 2008)

**Appendix 2** (*Continued*)

Type of indicators	St	Pr	Ot	References
Antihypertensive treatment was given when blood pressure $\geq 160/110$ mm Hg		X		
Respiratory rate and tendon reflexes monitored in women treated with magnesium sulphate		X		
Intravenous access and hydration was achieved in women with obstructed labor		X		
Antibiotic prophylaxis was given during caesarean delivery		X		
Intravenous access achieved and crystalloids and/or colloids should be infused in women with postpartum haemorrhage		X		
Administration of uterotonics was recorded		X		
Malaria, diarrhoea and pneumonia				
Indicator for in/out patient treatment of malaria in adherence to standard treatment guideline (STG)		X		(Vang <i>et al.</i> 2006; Chareonkul <i>et al.</i> 2002; Wahlstrom <i>et al.</i> 2003)
Indicator for in/out patient treatment of pneumonia in adherence to STG		X		
Indicator for in/out patient treatment of diarrhoea in adherence to STG		X		
Percentage of children $<5$ with ARI given antibiotics		X		
Asthma				
Preventer (corticosteroid inhalers) - reliever (short-acting beta agonist inhalers) prescription ratio in asthma treatment		X		(Chong <i>et al.</i> 2008)
Diabetic				
Antiplatelet therapy to prevent cardiovascular disease in diabetic patients over age 40 year old		X		(Kanchanaphibool <i>et al.</i> 2009)
Psychosis				
Patients hospitalised for an acute episode of psychosis and prescribed an antipsychotic medication on discharge		X		(Chong <i>et al.</i> 2006)
Patients treated with antipsychotic medication for at least three months and received a medication adjustment following persistent psychotic symptoms or antipsychotic-related side effects		X		
Patients discontinued from antipsychotic medications and have a documented plan for recognizing and responding to signs of relapse		X		
Patients who had at least four medication or psychotherapy visits with a psychiatrist within a year from first visit		X		
Patients treated with antipsychotic medication and evaluated for medication side effect within three months of prescription		X		
Patients who had either one inpatient admission or two outpatient visits for psychosis within a 12-month period and received education about their prescribed medications and side effects		X		
Patients prescribed oral antipsychotic drugs, reported medication non-compliance and received depot maintenance therapy		X		
Tuberculosis (TB)				
Percentage of smear-positive TB patients who received correct TB drugs in correct dosages		X		(Uchiyama <i>et al.</i> 2006)



**Appendix 2** (*Continued*)

Type of indicators	St	Pr	Ot	References
Percentage of new smear-positive TB out-patients with correct knowledge of TB treatment			X	
4. Others	2	0	0	
National Drug Policy (NDP)				
The use of standard treatment guidelines (STGs)	X			(Vang <i>et al.</i> 2006;
Drug and Therapeutics Committee (DTC)				Paphassarang <i>et al.</i> 2002)
DTC drug information	X			

St, structure; Pr, process; Ot, outcome; The classification of structure, process and outcome indicators based on the aspect of care as described by Donabedian.

Full lists of indicators used in original articles were not shown; only indicators relating to quality use of medicines were reported.

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